EXHIBIT A

The opinion in support of the decision being entered today
is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte AVI J. ASHKENAZI, KEVIN P. BAKER, DAVID A. BOTSTEIN, LUC DESNOYERS, DAN L. EATON, NAPOLEONE FERRARA, SHERMAN FONG, WEI-QIANG GAO, HANSPETER GERBER, MARY E. GERRITSEN, AUDREY GODDARD, PAUL J. GODOWSKI, AUSTIN L. GURNEY, IVAR J. KLJAVIN, JENNIE P. MATHER, MARY A. NAPIER, JAMES PAN, NICHOLAS F. PAONI, MARGARET ANN ROY, TIMOTHY A. STEWART, DANIEL TUMAS, COLIN K. WATANABE, MICKEY P. WILLIAMS, WILLIAM I. WOOD, and ZEMIN ZHANG

Appeal 2007-1149
Application 10/066,273
Technology Center 1600

Decided: June 7, 2007

Before TONI R. SCHEINER, ERIC GRIMES and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an antibody. The Examiner has rejected the claims for lacking utility. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

BACKGROUND

The Specification describes a clone "isolated from a human fetal lung library using a trapping technique which selects for nucleotide sequences encoding secreted proteins" (Specification 65). The Specification states that this "clone encodes a secreted factor," which is designated PRO444 (*id.*), and that the amino acid sequence of SEQ ID NO: 9 was derived from the coding sequence of this clone (*id.* at 27).

The Specification states that, as demonstrated by a positive result in the assay described in Example 60, PRO444 "act[s] to induce the expression of c-fos in pericyte cells" (*id.* at 142). The Specification also states that "[i]nduction of c-fos expression in pericytes is . . . indicative of the induction of angiogenesis and, as such, PRO polypeptides capable of inducing the expression of c-fos would be expected to be useful for the treatment of conditions where induced angiogenesis would be beneficial including, for example, wound healing, and the like" (*id.*).

In addition, the Specification describes "an antibody which specifically binds to" the described polypeptides (*id.* at 22). "Anti-PRO antibodies . . . are useful for the affinity purification of PRO from recombinant cell culture or natural sources" (*id.* at 99).

DISCUSSION

1. CLAIMS

Claims 40-44 are pending and on appeal. We will focus on claim 40, the broadest claim on appeal, which reads as follows:

> 40. An antibody that specifically binds to the polypeptide of SEQ ID NO:9.

2. REFERENCES

The Examiner relies on the following references:

L. Diaz-Flores et al., "Angiogenesis: an update," 9 *Histol. Histopath.*, 807-843 (1994).

Ralf Janknecht et al., "Signal integration at the c-*fos* promoter," 16 *Carcinogenesis*, 443-450 (1995).

Daniel G. Herrera et al. , "Activation of *c-fos* in the Brain," 50 *Progress in Neurobiology*, 83-107 (1996).

Maurizio Orlandini et al., "Identification of a c-*fos*-induced gene that is related to the platelet-derived growth factor/vascular endothelial growth factor family," 93 *Proc. Natl. Acad. Sci.*, 11675-11680 (1996).

Krisztina Kovács, "c-Fos as a transcription factor: a stressful (re)view from a functional map," 33 *Neurochem. Int.*, 287-297 (1998).

Vincent Coulon et al., "A Novel Calcium Signaling Pathway Targets the c-*fos* Intragenic Transcriptional Pausing Site," 274 *J. Biol. Chem.*, 30439-30446 (1999).

Atsushi Otani et al., "Angiotensin II-Stimulated Vascular Endothelial Growth Factor Expression in Bovine Retinal Pericytes," 41 *Investigative Ophthalmology & Visual Science*, 1192-1199 (2000).

Shinichi Sakurai et al., "Retinal Capillary Pericyte Proliferation and c-*Fos* mRNA Induction by Prostaglandin D_2 through the cAMP Response Element," 43 *Investigative Ophthalmology & Visual Science*, 2774-2781 (2002).

Ugur Ozerdem, et al. "Early Contribution of Pericytes to Angiogenic Sprouting and Tube Formation," 6 *Angiogenesis*, 241-249 (2003).

3. UTILITY

Claims 40-44 stand rejected under 35 U.S.C. § 101 as lacking patentable utility. The Examiner argues that the "application has provided a description of an isolated protein and an antibody to this protein," but that it "does not disclose a specific biological role for the[] protein and antibody or their significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect" (Answer 3).

The Examiner acknowledges that the Specification states that anti-PRO antibodies are "useful for the affinity purification of PRO," but argues that, "because at the time of filing of the instant application the specific and substantial credible utility of the PRO444 polypeptide[] was not established, there appears to be no pressing practical need to use the claimed antibodies to isolate PRO444" (*id.* at 5-6). Rather, "[t]o use an antibody to polypeptide PRO444 of the instant invention in any of the disclosed methods would clearly be using it as the object of further research" (*id.* at 6).

Appellants argue that "the claimed antibodies are useful in the purification of PRO444 polypeptides, which in turn have utility . . . as stimulators of angiogenesis" (Br. 7). Appellants cite the results shown in the Specification's Example 60, which states that PRO444 "act[s] to induce the expression of c-fos in pericyte cells," and that "[i]nduction of c-fos expression in pericytes is . . . indicative of the induction of angiogenesis and, as such, PRO polypeptides capable of inducing the expression of c-fos would be expected to be useful for the treatment of conditions where

induced angiogenesis would be beneficial including, for example, wound healing" (Specification 142).

Section 101 requires a utility that is both substantial and specific. A substantial utility requires "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." *In re Fisher*, 421 F.3d 1365, 1371, 76 USPQ2d 1225, 1230 (Fed. Cir. 2005). A specific utility is "a use which is not so vague as to be meaningless." *Id.* In other words, "in addition to providing a 'substantial' utility, an asserted use must also show that [the] claimed invention can be used to provide a well-defined and particular benefit to the public." *Id.*

"[T]he PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility." *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (citation omitted).

In this case, we agree with Appellants that the Examiner has not provided a sufficient basis to challenge the Specification's assertion of utility. We agree with the Examiner that the art demonstrates that a variety of stimuli may activate c-fos and that not all of these stimuli are necessarily involved in cancer or pathogenic angiogenesis. In particular, it is not clear

that Appellants have demonstrated that PRO444 is involved in cancer or pathogenic angiogenesis, and therefore that inhibition of PRO444 would be effective in these conditions.

However, Appellants have provided an assay indicating that PRO444 "act[s] to induce the expression of c-fos in pericyte cells" (Specification 142). The Specification states that polypeptides having this activity "would be expected to be useful for the treatment of conditions where induced angiogenesis would be beneficial including, for example, wound healing" (*id.*).

The references cited by the Examiner support Appellants' position that inducers of c-fos expression in pericytes stimulate angiogenesis. In particular, Sakurai indicates that its findings "support the view that . . . induction of c-*fos* mRNA is an important step in the induction of VEGF expression in retinal pericytes," VEGF being "a key growth factor for retinal neovascularization" (Sakurai 2779-2780). In addition, we do not agree with the Examiner that Sakurai demonstrates that "not all the factors that activate *c-fos* . . . induce VEGF" (Answer 12). As noted by the Examiner, Sakurai states that several prostaglandins induced c-fos mRNA (Sakurai 2777) and that one of them, PGD_2, was shown to induce VEGF mRNA (*id.* at 2779). However, we agree with Appellants that Sakurai does not state that the other prostaglandins do *not* induce VEGF mRNA (Br. 15-16). Instead, there is no indication in Sakurai that the effect of these other prostaglandins on inducing VEGF mRNA was tested.

In addition, Otani indicates that Angiotensin II (AII) "induces VEGF in retinal microcapillary pericytes" and "is reported to stimulate the

expression of c-*fos* and c-*jun* and their respective proteins, c-Fos and c-Jun, which constitute the heterodimer complex called AP-1" (Otani 1196-1197). Otani states that the data "suggest a predominant role of AP-1 . . . in AII induction of VEGF" in bovine retinal microcapillary pericytes (*id.* at 1977). Thus, both Sakurai and Otani appear to support Appellants' position that inducers of c-fos expression in pericytes stimulate angiogenesis. (Br. 14-18.)

Therefore, we agree that those skilled in the art would reasonably accept the Specification's assertion that PRO444 is a stimulator of angiogenesis. The Examiner has provided no basis for doubting that stimulating angiogenesis is useful in, for example, wound healing, and therefore is a specific and substantial utility.

The Examiner cites Orlandini as disclosing that VEGF expression in fibroblasts is unaffected by c-fos. We disagree. Granted, Orlandini states that, "*in vitro*, the VEGF mRNA level is not affected by c-*fos*" (Orlandini 11680). However, Orlandini recognizes that this is in contrast with observations that VEGF mRNA "is elevated in papillomas originating from c-*fos* wild-type cells with respect to papillomas originating from c-*fos*-deficient cells" (*id.*). Orlandini concludes that "[i]t is likely that other events must happen before VEGF is induced during tumor progression since this effect can only be observed *in vivo*" (*id.*). Thus, we agree with Appellants (Br. 20-21) that Orlandini does not disclose that expression of c-fos in fibroblasts is unaffected by c-fos, merely that it is unaffected *in vitro*.

The Examiner cites Diaz-Flores and Ozerdem as evidence that "the involvement of pericytes in angiogenesis is controversial and not fully

understood" (Answer 13) and that "although pericytes play [an] important role in angiogenesis, their role in formation of tumor neovasculature is currently not fully understood" (*id.* at 9-10).

We agree that Diaz-Flores and Ozerdem suggest that the role of pericytes in angiogenesis was not entirely elucidated at the time of Appellants' invention. However, both of these references confirm that pericytes are involved in angiogenesis (Diaz-Flores 809, "Events of new blood vessel formation"; Ozerdem 246 ("we observe pericytes and endothelial cells working in concert to form angiogenic microvessels")). In addition, the Examiner has not pointed to any teaching in either of these references indicating that *inducers* of c-fos expression do not *stimulate* angiogenesis.

We conclude that the Examiner has not provided a sufficient basis to reasonably doubt that "[i]nduction of c-fos expression in pericytes is . . . indicative of the induction of angiogenesis" or that "polypeptides capable of inducing the expression of c-fos would be expected to be useful for the treatment of conditions where induced angiogenesis would be beneficial" (Specification 142). Therefore, we agree with Appellants that the Examiner has not provided an adequate basis to reasonably doubt the assertion that "the claimed antibodies are useful in the purification of PRO444 polypeptides, which in turn have utility . . . as stimulators of angiogenesis" (Br. 7). We therefore reverse the utility rejection of claims 40-44.

4. ENABLEMENT

Claims 40-44 stand rejected under 35 U.S.C. § 112, first paragraph, because, in view of the lack of utility, "one skilled in the art . . . would not

know how to use the claimed invention" (Answer 6). Because we are reversing the utility rejection, we also reverse the enablement rejection of claims 40-44.

SUMMARY

The Examiner has not adequately shown that the claims lack utility. We therefore reverse the rejections of claims 40-44.

REVERSED

Smsc

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